PCT/FR2003/002242

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BIE006405/WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/FR2003/002242	International filing date (*day/month/year*) 16 juillet 2003 (16.07.2003)	Priority date (*day/month/year*) 16 juillet 2002 (16.07.2002)
International Patent Classification (IPC) or national classification and IPC C07C 323/66		
Applicant INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06 février 2004 (06.02.2004)	04 November 2004 (04.11.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR2003/002242

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-22, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:

pages 1-4, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the drawings:

pages 1/1, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-4	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-4	NO
Industrial applicability (IA)	Claims	1-4	YES
	Claims		NO

2. Citations and explanations

Reference is made to the following documents:

D1: WO99/36066 A (Institut National de la Santé et de la Recherche médicale, et al) 22 July 1999

D2: WO96/18609 A (Procept) 20 June 1996

1. **Subject Matter**

The present application relates to two 4,4'-dithiobis[3-aminobutane-1-sulphonic] acid derivatives, the disodium salt and the diester of 2,2-dimethylpropyl and the use thereof for treating hypertension.

2. **Novelty**

Document D1 describes (claims 1 and 3) the use of a sodium (S)-3-amino-4-mercaptobutanesulphonate compound to reduce blood pressure. The two compounds according to the present invention are not described in D1 or in other prior art documents. Consequently, the present application meets the requirements of PCT Article 33(2), since the subject matter of claims 1-4 is novel.

3. **Inventive Step**

Document D1, which is considered the prior art closest to the subject matter of claims 1-4, describes (claims 1 and 3) the use of sodium (S)-3-amino-4-mercaptobutanesulphonate to lower blood pressure. One of the compounds of the present application is the disulphide of said prior art compound.

It is impossible to compare the data relating to the biological activity of sodium (S)-3-amino-4-mercaptobutanesulphonate (D1, examples 1-5) with those of the compounds claimed in the present application. It is therefore impossible to determine the technical effect obtained by the use thereof for treating hypertension.

The problem that the present invention aims to solve can therefore be considered to be that of providing alternative compounds for treating hypertension. This problem is solved by the applicant by using the disulphide from sodium (S)-3-amino-4-mercaptobutanesulphonate and the disulphide from the 2,2-dimethylpropyl ester of 3-amino-4-mercaptobutanesulphonic acid.

A person skilled in the art is aware that, in general, a disulphide is easily converted *in vivo* into the corresponding thiol. It is also known (D2, page 3, line 15 to page 4, line 3) that a neopentyl ester (i.e. 2,2-dimethylpropyl) of a sulphonic acid is easily converted into the corresponding sulphonic acid. Consequently, in the absence of a surprising

effect resulting from the use of the two disulphides of the present application instead of the corresponding thiol of D1, an inventive step cannot be recognised, and the subject matter of claims 1-4 does not meet the requirements of PCT Article 33(3).